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April 6, 2011

VIA HAND DELIVERY ONLY
Honorable Patty Shwartz, U.S.M.J.
Frank R. Lautenberg U.S.P.O & Cthse. Bldg.
Rm. 477
Newark, New Jersey 07101

Re: *Nycomed US Inc., et al. v. Tolmar Inc.*
Civil Action No. 10-2635 (KSH)(PS)

Dear Judge Shwartz:

Pursuant to the Court's direction on the March 31 teleconference, Plaintiffs Nycomed US Inc. and Jagotec AG (collectively, "Plaintiffs") and Defendant Tolmar Inc. ("Tolmar") submit this joint letter concerning whether the April 8, 2010 letter from Tolmar to Plaintiffs giving notice of Tolmar's Paragraph IV certification for the Patents-in-Suit (hereinafter "Paragraph IV notice letter") is confidential.[1] **We respectfully request that the Court not file this submission on the public docket, as it contains Confidential information.**

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[1] Plaintiffs informed Tolmar on April 1 that they were reserving a portion of their two pages for a very short reply section (identified as "Plaintiffs' Reply" below), which Plaintiffs understood to have been contemplated by the Court when it set a schedule that permitted Plaintiffs to file a letter by 2 p.m. the day after receiving Tolmar's section of the joint letter. When Tolmar provided its response four days later, it objected for the first time to Plaintiffs' inclusion of a reply paragraph. Plaintiffs have not altered their initial portion of this letter, however, in any respect.

I. Plaintiffs' Position

The Court asked Plaintiffs to address whether a Paragraph IV notice letter is confidential or publicly available. Such letters, once provided to the patent holder or the New Drug Application (NDA) holder, are considered public disclosures under controlling authority.

The requirements for Paragraph IV notice letters arise under the Federal Food, Drug and Cosmetic Act ("FDCA") and Food and Drug Administration ("FDA") regulations. The FDA has long explained that "paragraph IV certifications are subject to public disclosure under the Freedom of Information Act (FOIA)" and further that a Paragraph IV notice letter constitutes "***a public disclosure*** once [it] has been provided to the [New Drug Application] holder and the patent holder." 68 Fed. Reg. 36676, 36690 (June 18, 2003) (emphasis added). Deference is owed to the FDA's interpretation of the FDCA and its regulations.[2]

The FDA recently considered the very question we have here and held that a Paragraph IV notice provided to a patent holder is a public disclosure. (*See* Exhibit A, highlighting pertinent passages). Notably, the FDA rejected the contention that a Paragraph IV notice letter "is considered trade secret and confidential commercial information" even where it contains detailed information about the composition of the drug product. (*Id.* at 4-5.) In a section titled "Paragraph IV Notice Letter is a Public Disclosure," the FDA noted the "intrinsically public nature of paragraph IV notice letters" (*id.* at 6) and explained that "[s]ubmitting a paragraph IV certification in an ANDA, and providing the corresponding notice of such certification … reflects a deliberate decision by an ANDA applicant to publicly disclose certain information about its ANDA" (*id.* at 5). The FDA thus concluded the Paragraph IV letter, despite containing detailed composition information, should be available on the FDA's public docket (*id.* at 1). This FDA ruling is also entitled to deference. *Mylan Labs, Inc. v. Thompson*, 389 F.3d 1272, 1279-1280 (Fed. Cir. 2004) (applying "*Chevron*" deference to FDA letter ruling).

Thus, under clear authority, Tolmar's Paragraph IV notice letter is considered a public disclosure of the information contained within that letter. Tolmar has not suggested—and certainly could not establish—that the FDA's conclusion on this issue is an impermissible interpretation of the FDCA and FDA regulations.

Moreover, Tolmar's position flies in the face of clear industry custom. As the FDA ruling notes, "established practice within the generic and innovator drug industry reflects the public nature of paragraph IV notice letters." (Ex. A at 6.) Such letters are "routinely publicly disclosed by NDA sponsors as attachments to citizen petitions or as attachments to complaints

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[2] *See, e.g., Novartis Pharms. Corp. v. Leavitt*, 435 F.3d 344, 349 (D.C. Cir. 2006) ("FDA interpretations of the [FDCA] receive deference, as do its interpretations of its own regulations unless plainly erroneous or inconsistent with the regulations." (citations omitted)); *accord NVE, Inc. v. HHS*, 436 F.3d 182, 186 (3d Cir. 2006) (citing, *inter alia*, *Chevron U.S.A., Inc. v. NRDC, Inc.*, 467 U.S. 837, 842-43 (1984)).

in patent infringement litigation." (*Id.* at 6.) As the FDA put it, "The historic public availability of … paragraph IV notice letters undercuts any claim that there is a reasonable basis to assume that information shared with" the recipients of a Paragraph IV notice letter "will remain confidential and exempt from further disclosure." (Ex. A at 6.)

Tolmar sent its Paragraph IV letter, unsolicited, to its competitors, including a company (SkyePharma) that is not a party to this litigation. Indeed, Tolmar sent the letter to individuals at Nycomed and Jagotec who are not even eligible to receive highly confidential information under the Discovery Confidentiality Order (DCO), which of course did not exist when Tolmar sent its letter. When Tolmar sent the letter, there was no certainty of litigation, much less particular terms of a DCO. Tolmar's deliberate act of sending the letter to these competitors is inconsistent with any assertion that the letter should be protected from disclosure. Indeed, were there any particular information that Tolmar had wished to keep secret, Tolmar could have excluded it from the Paragraph IV notice letter and instead produced it only pursuant to an Offer of Confidential Access. See 21 U.S.C. § 355(j)(5)(C)(i)(III). Many Paragraph IV notice letters issued by generic drug companies simply say that their proposed product does not meet certain elements of the listed patents. Tolmar chose not to do this. It instead elected to share the information with Nycomed, Jagotec, and SkyePharma, and should not now be permitted to limit those companies' use or disclosure of the information.

Thus, Tolmar's confidentiality claim over its Paragraph IV letter lacks any merit under controlling authority. Having already publicly disclosed the letter to Plaintiffs, the Paragraph IV notice letter does not qualify for protection as confidential information under the terms of the Discovery Confidentiality Order. (*See* D.I. 59 ¶ 15.) Therefore, Plaintiffs request that the Court rule that the Paragraph IV notice letter is not confidential, including under the DCO.

Plaintiffs' Reply: Below, Tolmar relies on an OCA not accepted by Plaintiffs, D.I. 13-1 ¶¶ 7-11. (Tolmar also purports to rely on the DCO, but that did not exist when Tolmar sent the notice letter.) It is well established, however, that an OCA is inapplicable to a notice letter. (*See, e.g.*, Ex. A at 8 (section 355(j)(5)(C)(i)(III) "is intended to protect the confidentiality of information contained in an ANDA, and *not to protect information contained in a paragraph IV notice letter*.").)[3] FDA further explained that a notice letter is a public disclosure even if marked "confidential." (*Id.* at 7-8.) Finally, it is irrelevant that in sending its Paragraph IV notice letter, Tolmar identified the detailed statement as an enclosure (which is incorporated by reference into the letter, *see* Ex. C at TOL_11443). For the reasons FDA identified, the materials sent to the patent holder and NDA holder are public disclosures.

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[3] Whether Tolmar has provided the notice letter to FDA is irrelevant. The Federal Register not only speaks of the availability of a *certification* through FOIA, but also declares that a Paragraph IV notice letter is a "public disclosure," which thus can be used freely by recipients.

II. Tolmar's Position

Tolmar's Paragraph IV Notice Letter and Separate OCA – On April 8, 2010, Tolmar sent Plaintiffs: (i) a Paragraph IV Notice Letter (Ex. B), and (ii) a 27-page Offer of Confidential Access ("OCA"), containing a detailed statement of the bases of Tolmar's non-infringement position (Ex. C, pp. 5-27).[4] The OCA expressly invoked the confidential access provision of 21 U.S.C. § 355(j)(5)(C)(i)(III) ("A request for access to an application under an offer of confidential access *shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access*, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract").[5]

Tolmar prominently marked its OCA with detailed statement as "Confidential," and specifically stated that "[w]hile the litigation is pending, portions of the ANDA provided . . . or other documents to the extent that they contain information in the ANDA, shall be treated as information under the highest level of confidentiality under any protective order entered in the action brought against TOLMAR." (Ex. C, p. 2). The OCA further stated: "THIS CONFIDENTIALITY APPLIES TO THIS STATEMENT, WHICH MAY NOT, AND SHOULD NOT, BE ATTACHED TO ANY COMPLAINT OR OTHER PUBLICLY AVAILABLE DOCUMENT." *Id.* at p. 5. Subject to these protections, Tolmar disclosed confidential ANDA product formulation components in the OCA's detailed statement with an expectation that the information would be treated confidentially. Tolmar did not disclose confidential formulation components in its Paragraph IV Notice Letter.

Tolmar subsequently produced its Paragraph IV Notice Letter and OCA with detailed statement (Production Nos. TOL0000011466-11468 and TOL0000011439-465) on October 15, 2010, bearing an additional "CONFIDENTIAL" designation consistent with that prescribed by the mutually agreed DCO entered by the Court. For over five months, Plaintiffs never challenged the "CONFIDENTIAL" designation.

Plaintiffs Mischaracterize the FDA Letter (Exhibit A) – Contrary to Plaintiffs' assertion, neither the FDA nor any other authority has so broadly determined that Paragraph IV Notice Letters are *per se* public disclosures. Instead, the FDA merely found a public disclosure under a particular set of facts, which are not found here. There, Altana's Paragraph IV Notice Letter failed to invoke the confidential access provision of the Hatch-Waxman Act, 21 U.S.C. § 355(j)(5)(C)(i)(III). The FDA letter found this failure to be a significant factor in denying Altana's request for confidentiality. (Ex. A, pp. 4, 5 n.5). Altana also combined its detailed

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[4] On page 3 of this letter, Plaintiffs fault Tolmar for sending its Paragraph IV Notice Letter to SkyePharma. Yet, Plaintiffs fail to advise the Court that: (i) co-plaintiff Jagotec is a subsidiary of SkyePharma, the original NDA holder, and (ii) SkyePharma's website characterizes the drug at issue, Solaraze,® as "[o]ur proprietary hyaluronic acid gel technology." (Ex. D).

[5] Plaintiffs requested access to Tolmar's ANDA and other confidential business information shortly after receiving Tolmar's Paragraph IV Notice Letter and 27-page OCA (Ex. B, C). Per § 355(j)(5)(C)(i)(III), Plaintiffs' request constituted acceptance of Tolmar's OCA terms.

statement with its Notice Letter and failed to include an OCA outlining terms for treatment of any confidential business information. Based on these facts, the FDA found that Altana did not have an expectation of confidentiality when it sent its Notice Letter to the NDA holder. *Id.* at p.1.

In contrast to Altana, Tolmar (1) expressly invoked 21 U.S.C. § 355(j)(5)(C)(i)(III) and its confidentiality provisions; and (2) provided a separate 27-page OCA which unambiguously demonstrates Tolmar's confidentiality expectations by stating that the OCA "contain[s] information in the ANDA, [which] shall be treated as information under the highest level of confidentiality under any protective order entered in the action brought against TOLMAR." (Tolmar OCA, Ex. B, p. 2). Thus, the FDA letter upon which Plaintiffs rely (Ex. A) is irrelevant here. Further, this Court has recognized Tolmar's confidentiality expectations of its formulation components and the resulting injury to Tolmar from public disclosure:

> The Court . . . finds that . . . there is a legitimate reason to at least at this point seal limited portions of paragraphs 66, 70 through 74 and 76 [of the Complaint] that disclose formulation information of the proposed ANDA product. Having this information so easily available to the public could pose a competitive disadvantage. While the record seems to suggest that the defendant made a knowing decision to make a disclosure to a group of eight corporations or public officials, ***it did so with the expectation that at least it was being disclosed to them confidentially***. . . . Moreover, the Court finds that the defendant's intention at that time was to make a limited disclosures to those -- only those implicated and not a disclosure to the world at large.

(May 28, 2010 Hearing, Dkt. 17, 25:7-26:22) (emphasis added). The confidential formulation disclosed in Tolmar's detailed statement mirrors the information disclosed in Tolmar's ANDA, which is confidential business information under the DCO. Plaintiffs have provided no legitimate reason why the Paragraph IV Notice Letter and the OCA's detailed statement should be exempt from the DCO's confidentiality provisions entered by the Court.

Tolmar's Paragraph IV Notice Letter Is Not Accessible Through FOIA – Plaintiffs distort the FDA regulations and scope of FOIA. The FDA "decline[d] to amend the proposed rule to make public all paragraph IV certifications . . . ." 68 Fed. Reg. 36690 (June 18, 2003). Here, Tolmar did not file its Paragraph IV Notice Letter or the OCA with detailed statement with the FDA. Instead, Tolmar satisfied its statutory obligations under the Hatch-Waxman Act by filing a certification and proof of service of its Paragraph IV Notice Letter with the FDA. (Ex. E). FOIA only pertains to information maintained by a governmental agency. In the absence of the requested information, the FDA has nothing to disclose. Thus, even if Plaintiffs were to submit a FOIA request, neither the Paragraph IV Notice Letter nor the OCA with detailed statement would be publicly available as they were never filed with the FDA. Accordingly, Plaintiffs' argument that Paragraph IV Notice Letters are generally subject to public disclosure under FOIA is unavailing.

For these reasons, Tolmar respectfully requests that this Court preserve the confidentiality of Tolmar's formulation disclosed in the OCA's detailed statement pursuant to both the OCA and DCO.

Respectfully submitted,

Leda Dunn Wettre

Leda Dunn Wettre

Attachment

cc: Counsel of Record (via email)

EXHIBIT A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JAN 7 2010

Areta L. Kupchyk, Esq.
Reed Smith LLP
1301 K Street, N.W.
Suite 1100 – East Tower
Washington, DC 20005-3373

Dear Ms. Kupchyk:

I am writing in response to your letters of October 6, October 26, and December 11, 2009, on behalf of Nycomed U.S. Inc. (Nycomed) requesting that the Food and Drug Administration (FDA or Agency) immediately remove Graceway Pharmaceuticals, Inc.'s (Graceway) Citizen Petition dated August 28, 2009, Docket No. FDA-2009-P-0423, (Citizen Petition) and its attached exhibits from the public docket. In your letters, you assert that the Citizen Petition contains confidential and proprietary information from Nycomed's abbreviated new drug application (ANDA) No. 78-548 and that this information is protected from disclosure under the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) and FDA's regulations. On October 9, 2009, FDA notified you by letter that the Agency had removed the Citizen Petition and attached exhibits from the public docket pending resolution of the issue. We have now carefully considered your request and, as explained below, disagree with your assertion that the Citizen Petition and its attached exhibits are protected from disclosure by FDA. Accordingly, we intend to re-post Graceway's Citizen Petition and its attachments in the public docket on Wednesday, January 13, 2010, at approximately 5:00 pm.

I. Background

Altana (now Nycomed)[1] submitted ANDA 78-548 to FDA seeking approval for a generic imiquimod cream 5%. As part of its application, Altana submitted a certification pursuant to § 505(j)(2)(A)(vii)(IV) of the Act, stating that U.S. Patent No. 5,238,944 (the '944 Patent), covering Aldara®, the drug referenced by its ANDA, is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Nycomed's product (paragraph IV certification). Pursuant to § 505(j)(2)(B)(ii) and 21 C.F.R. § 314.95, Nycomed also provided notice to Graceway, the sponsor (or "holder") of the new drug application (NDA) for Aldara, of the paragraph IV certification and a detailed statement of the factual and legal bases for Nycomed's opinion that the '944 Patent will not be infringed (Nycomed paragraph IV notice letter). This letter included detailed information about the manufacture and composition of Nycomed's

[1] Altana was subsequently purchased by Nycomed and renamed Nycomed US Inc. For the purposes of this letter, Altana will hereinafter be referred to as Nycomed.

product.[2] The Nycomed paragraph IV notice letter also stated that the information contained in the notice is confidential.

On August 28, 2009, Graceway submitted to FDA the Citizen Petition, requesting, among other things, that FDA refuse to approve Nycomed's ANDA, and require the application to be submitted as an NDA under § 505(b)(2). Graceway referenced the information contained in the Nycomed paragraph IV notice letter in the Citizen Petition and attached a copy of this notice letter to the Citizen Petition.[3] Pursuant to 21 C.F.R. § 10.30 and § 10.20, citizen petitions are publicly available through FDA's Division of Dockets Management. Under FDA's practice, citizen petition dockets are also available electronically at www.regulations.gov. Consistent with this practice, FDA made the Graceway Citizen Petition publicly available through the Division of Dockets Management and on www.regulations.gov

Nycomed subsequently discovered that its paragraph IV notice letter was in the public docket for the Citizen Petition and noted the issue for FDA at a meeting on October 1, 2009 with staff from the Office of Chief Counsel and the Center for Drug Evaluation and Research (CDER). On October 6, 2009, you requested by letter that FDA remove the Citizen Petition and its attached exhibits from the public docket on the ground that they impermissibly disclosed Nycomed's confidential information. By letter dated October 9, 2009, the Agency notified you that it had removed the Citizen Petition and its attached exhibits from public display pending resolution of the issue.

Philip Katz, on behalf of Graceway, submitted a letter to FDA on October 16, 2009, asserting that the Nycomed paragraph IV notice letter is not confidential because it was shared with Graceway, a competitor, without any protection, and requesting a meeting with Michael Landa, the Agency's Acting Chief Counsel. FDA received your letter of October 26, 2009, responding to Mr. Katz's letter. On November 3, 2009, Mr. Katz, other attorneys from his law firm, Hogan & Hartson, and representatives from Graceway met with Mr. Landa and attorneys in the Office of Chief Counsel. Mr. Katz submitted another letter on November 18, 2009, on behalf of Graceway, replying to your October 26, 2009, letter. On December 11, 2009, you wrote to Mr. Landa, providing comments on Mr. Katz's letter and requesting the opportunity to meet with FDA's Office of Chief Counsel. This request was granted, and you and your client met with staff from the Office of Chief Counsel and CDER on December 22, 2009.

II. Relevant Statutory and Regulatory Provisions

The issue you raise requires consideration of provisions related both to the generic drug approval process and to the confidentiality of ANDAs and other information submitted to federal agencies such as FDA. A summary of the relevant provisions is set forth below.

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[2] For example, Nycomed included in its paragraph IV notice letter formulation records. We note that portions of these formulation records were redacted by Nycomed before they were provided to Graceway.

[3] Graceway's Citizen Petition also requested that the Agency refuse to approve the ANDA submitted by another company, Perrigo, and attached a copy of the paragraph IV notice letter provided to Graceway by Perrigo. The confidentiality of Perrigo's notice letter is not at issue here.

Section 505(j) of the Act establishes the ANDA approval process, which permits generic versions of previously approved innovator drugs to be approved without submitting a full NDA. An ANDA must include a certification for each of the patents listed by the sponsor of the NDA for the drug referenced by an ANDA in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book). § 505(j)(2)(A)(vii). If an ANDA applicant intends to market its product before the expiration of a relevant patent and believes that the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the product covered by the ANDA, it is required to submit a certification to this effect to FDA (paragraph IV certification). § 505(j)(2)(A)(vii)(IV).

A paragraph IV certification begins a process in which the question as to whether the listed patent is valid, unenforceable, or will be infringed by the proposed generic product may be answered by the courts before the expiration of the patent. The ANDA applicant must provide the sponsor of the NDA for the referenced drug and the patent owner notice of the submission of the paragraph IV certification and a detailed statement of the factual and legal bases for the applicant's opinion that the patent in question is invalid, unenforceable, or will not be infringed (paragraph IV notice letter). § 505(j)(2)(B); 21 C.F.R. § 314.95. This notice letter alerts the NDA sponsor and patent owner of the submission of the ANDA for which approval is sought before the patent expires and provides them with the opportunity to enforce their patent rights by filing a patent infringement action. If the NDA sponsor or patent owner brings a patent infringement action within 45 days of receipt of the paragraph IV notice letter, with certain exceptions not relevant here, the approval of the ANDA may not made effective until at least 30 months from the date of receipt of the paragraph IV notice letter. § 505(j)(5)(B)(iii); 21 C.F.R. § 314.107(b)(3)

The notice letter to the NDA sponsor and patent owner is required under § 505(j)(2)(B)(iv) to be a "detailed statement of the legal and factual basis of the opinion of the applicant that the patent is invalid or will not be infringed." In addition, the Act provides a "confidential access" mechanism for an ANDA applicant to share more detailed information in its ANDA with the NDA sponsor or patent owner while also restricting access to, and imposing limitations on the use or the disposition of, that confidential information. Section 505(j)(5)(C)(i)(III) sets forth a specific procedure for this process. This procedure is triggered initially by the ANDA applicant including with its paragraph IV notice letter an offer of confidential access to its ANDA for the purposes of determining whether a patent infringement action should be brought. § 505(j)(5)(C)(i)(III). If the offer of confidential access is included with an ANDA applicant's paragraph IV notice letter, and certain other conditions are met, the ANDA applicant is permitted to seek a declaratory judgment with respect to the patent which is the subject of its paragraph IV certification. § 505(j)(5)(C)(i)(II). Under this provision, a request by the recipient of the notice letter for access to the ANDA shall be considered acceptance of the offer of confidential access. § 505(j)(5)(C)(i)(III). Thus, if an ANDA applicant wishes to share sensitive information in its ANDA, § 505(j)(5)(C)(i)(III) sets forth a very specific procedure under which the applicant is to allow the NDA sponsor or patent owner to review its ANDA, while maintaining the confidentiality of the information contained in it.

Additionally, there are several federal statutes relevant to the consideration of the confidentiality of information submitted to a federal agency such as FDA. The Freedom of Information Act

(FOIA) provides an exemption from its general disclosure mandate for "trade secrets" and "commercial or financial information obtained from a person [that is] privileged or confidential" (confidential commercial information). 5 U.S.C. § 552(b)(4) (Exemption 4). The Trade Secrets Act, which courts have interpreted to be at least coextensive with the scope of Exemption 4,[4] provides criminal liability for the disclosure of trade secret and/or confidential commercial information, unless authorized by law. 18 U.S.C. § 1905. More limited in scope, § 301(j) of the Act prohibits the disclosure outside of the Department of Health and Human Services (except under limited circumstances not applicable here) of trade secret information acquired under the authority of various provisions of the Act, including § 505. FDA's regulations also prohibit the disclosure of trade secrets and confidential commercial information. *See, e.g.*, 21 C.F.R. § 20.61(c). However, none of these statutory and regulatory provisions apply to information that has been publicly disclosed by its owner, and thus is neither secret or confidential.

III. Discussion

You assert that the information contained in the Nycomed paragraph IV notice letter is considered trade secret and confidential commercial information, as the terms are defined in FDA's regulations at 21 C.F.R. § 20.61(a) and (b). You further assert that, under the Trade Secrets Act and FDA's regulations, the information is protected from disclosure by FDA.

You acknowledge that Nycomed provided the paragraph IV notice letter to a third party, Graceway, and that it contained the information at issue. However, you assert that disclosure of information in a paragraph IV notice letter does not render the information "previously... published or made generally available," and therefore the information still falls within § 20.61's prohibition on disclosure. You also argue that, because the paragraph IV notice letter identified the information it contained as confidential, Graceway was prohibited under § 505(j)(5)(C)(i)(III), and under the express conditions under which the information was provided, from further disclosing the information. In addition, you assert that § 301(j) of the Act also prohibited Graceway from disclosing the information contained in the paragraph IV notice letter.

In our view, you misstate the standard that FDA uses to determine whether the owner of information has maintained its confidentiality. You cite 21 C.F.R. § 20.61(f), but that provision does not apply here. Section 20.61(f) enumerates the circumstances under which, when FDA receives a request for an Agency record (i.e., a FOIA request), FDA is not obligated to provide notice of disclosure to the submitter prior to releasing the record. However, the current situation does not involve a request for an agency record, and therefore § 20.61(f) is inapplicable.

Furthermore, as explained in the preamble to FDA's regulations on patent certifications, paragraph IV notice letters are considered public disclosures. 68 Fed. Reg. 36676, 36690 (June 18, 2003). Nycomed's predecessor, Altana, disclosed the Nycomed paragraph IV notice letter, and the information in it, to a member of the public, Graceway. It did so without taking advantage of the process specifically set forth in § 505(j)(5)(C)(i)(III) for disclosing sensitive

[4] *See, e.g., CNA Fin. Corp. v. Donovan*, 830 F.2d 1132, 1140 (D.C. Cir. 1987).

information contained in its ANDA. Therefore, the Nycomed paragraph IV notice letter (and the information in it) has previously been publicly disclosed, and there is no basis for FDA's refusing to post in its public docket either the notice letter attached to Graceway's Citizen Petition, or any references to it in that petition.

A. Paragraph IV Notice Letter is a Public Disclosure

As FDA has explained in rulemaking, the Agency considers a paragraph IV notice letter to be "a public disclosure once the [it] has been provided to the NDA holder and patent owner." 68 Fed. Reg. 36676, 36690 (June 18, 2003). The statutory scheme outlined above requires that the paragraph IV notice letter be sent to one or more third parties to notify the recipient of "the factual and legal basis of the opinion of the applicant that the patent is invalid and will not be infringed." An ANDA applicant is required under the Act to send a paragraph IV notice letter to the NDA sponsor and patent owner *only if* the applicant wishes to market its generic product before the expiration of a patent claiming the drug referenced in its applications. Submitting a paragraph IV certification in an ANDA, and providing the corresponding notice of such certification to the NDA sponsor, therefore reflects a deliberate decision by an ANDA applicant to publicly disclose certain information about its ANDA so that it may be eligible for FDA approval of its generic drug product prior to the expiration of the relevant patent.

The paragraph IV notice letter is an integral part of a public process in that it alerts the recipient to the potential infringement of its patent and provides it with information to help it evaluate whether to pursue legal action against the ANDA applicant and thus delay the approval of the generic drug. The documents filed in such a lawsuit, including a complaint, are, by default, publicly available, notwithstanding the fact that it is possible to obtain a protective order to maintain the confidentiality of certain information. Thus, the statutory scheme contemplates that the paragraph IV notice letter is the first step in an inherently public process. The statutory scheme also specifically provides a separate means for protecting the confidentiality of information contained in an ANDA, a procedure that Nycomed did *not* utilize.[5] Therefore, under the terms of the statute, Nycomed's paragraph IV notice letter and the information in it has been publicly disclosed, and under FDA's regulations at §§ 10.30 and 10.20, FDA must post the notice letter in the public docket.

[5] At your meeting with the Agency on December 22, 2009, you asserted that Nycomed met the requirements of the confidential access provision by providing an offer of confidential access at the same time as it provided the information. By "collapsing" these two steps, you argued, Nycomed helped to accomplish the goals of the statute by expediting Graceway's evaluation of the merits of its claims of non-infringement before the end of the 45-day period during which Graceway could sue Nycomed for infringement and obtain a 30-month stay of approval of Nycomed's ANDA. We find this argument unpersuasive. Simultaneously providing an offer of confidential access with the information itself does not allow the recipient the opportunity to accept the offer by requesting access to the ANDA. Therefore, the process clearly set forth in the confidential access provision of the Act, which contemplates an offer of confidential access, acceptance of the offer by requesting access to the ANDA, and review of the ANDA, was not followed here. Furthermore, Nycomed's paragraph IV notice letter cites only § 505(j)(2)(B), the statutory provision governing such letters, and not § 505(j)(5)(C)(i)(III), the confidential access provision. Accordingly, as further elaborated upon in Part B of this section, we disagree with your claim that your paragraph IV letter constituted "a document providing [an] offer of confidential access" per § 505(j)(5)(C)(i)(III).

Given the intrinsically public nature of paragraph IV notice letters, it is not necessary for FDA to address the arguments presented by the parties concerning Graceway's alleged contractual obligations to Nycomed under common law, or whether any such contractual obligations are relevant under 21 C.F.R. § 20.81(a).[6]

Furthermore, established practice within the generic and innovator drug industry reflects the public nature of paragraph IV notice letters and, as such, Nycomed did not have a reasonable basis to believe that the information provided in the paragraph IV notice letter would retain its confidential status upon disclosure to Graceway. As noted above, FDA has made clear that it considers the notice of paragraph IV certification to be a public disclosure once it has been provided to the NDA holder and patent owner. 68 Fed. Reg. 36676, 36690 (June 18, 2003). Paragraph IV notice letters are routinely publicly disclosed by NDA sponsors as attachments to citizen petitions or as attachments to complaints in patent infringement litigation,[7] and NDA sponsors and patent owners regularly announce their receipt of paragraph IV notice letters in press releases and filings with the Securities and Exchange Commission.[8] The historic public availability of these and other paragraph IV notice letters undercuts any claim that there is a reasonable basis to assume that information shared with an NDA sponsor or patent owner in a paragraph IV notice letter will remain confidential and exempt from further disclosure or use by that NDA sponsor or patent owner.[9]

B. Graceway was Not Prohibited by the Confidential Access Provision of the Act from Disclosing the Paragraph IV Notice Letter

Nycomed claims that, through its paragraph IV notice letter, the company granted Graceway confidential access to the proprietary information from its application (and contained in the Nycomed paragraph IV notice letter) "for the sole and limited purpose of evaluating possible infringement of Graceway's '944 patent that is the subject of the Certification 'and for no other purpose.'" Under § 505(j)(5)(C)(i)(III) (the confidential access provision), Nycomed argues,

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[6] Whether or not there could be a private arrangement separate from the paragraph IV notice letter to protect the confidentiality of information contained in, or derived from, the ANDA is not before us, and we decline to opine on such a situation.

[7] *See, e.g.*, Citizen Petition filed by Arnold & Porter on behalf of Abbott Laboratories and Laboratoires Fournier, Docket No. 2004P-0386 (Aug. 31, 2004); Citizen Petition filed by Auxilium Pharmaceuticals, Inc., Docket No. FDA-P-0123-001/CP (Feb. 27, 2009); Citizen Petition filed by sanofi-aventis US, Docket No. FDA-2007-P-0182 (June 7, 2007). These documents are all publicly available via FDA's website and/or www.regulations.gov. Graceway also provided examples of patent infringement complaints or patent prosecution filings that included copies of paragraph IV notice letters.

[8] *See, e.g.*, Cephalon, Inc., "Form 8-K" (Nov. 2, 2009), available at http://www.sec.gov/Archives/edgar/data/873364/000110465909062546/a09-32847_18k.htm;Astra Zeneca International, "Crestor ANDA," available at http://www.astrazeneca.com/media/latest-press-releases/2007/5355?itemId=3891576; Shire Pharmaceuticals Group plc, "ADDERALL XR® - Additional Paragraph IV notice received from IMPAX Laboratories, Inc., for lower strengths," (Dec. 7, 2004) available at http://www.shire.com/shire/uploads/press/shire/Impax_lower_strengths_filing_071204.pdf.

[9] We note that Nycomed redacted portions of the information contained in its paragraph IV notice letter, which suggests that Nycomed understood that only this redacted information would remain confidential and that the rest of the information in the letter would be subject to public disclosure.

Graceway was prohibited from further disclosing the information contained in the paragraph IV notice letter. However, for the reasons set forth below, we believe that Nycomed's reliance on § 505(j)(5)(C)(i)(III) is unfounded.

First, by its terms, the confidential access provision protects only information contained in an ANDA, not information found elsewhere, such as in a paragraph IV letter. It applies only when a paragraph IV notice letter is accompanied by a document providing an "offer" of confidential access to the ANDA. § 505(j)(5)(C)(i)(III). The confidential access provision is separate from the provisions in § 505(j)(2)(B) related to paragraph IV notice letters. It provides specific conditions that must be met for an ANDA applicant to be eligible to pursue declaratory judgment against a patent owner for non-infringement, namely, that the ANDA applicant offer the NDA sponsor and patent owner the opportunity to review its ANDA. Unlike the provisions related to paragraph IV notice letters, the confidential access provision expressly provides a procedure under which the ANDA applicant can take steps to protect the confidentiality of the information it shares with an NDA sponsor or patent owner. Where, as here, Congress has provided for confidentiality in one setting, but not in another, it is reasonable to conclude that Congress did not intend for paragraph IV notice letters to be considered confidential. *See, e.g.*, 2A Norman J. Singer & J.D. Shamble Singer, *Statutes and Statutory Construction* § 46:5 (7th ed. 2007) (It is a well-established canon of statutory construction that "where the legislature has employed a term in one place and excluded it in another, it should not be implied where excluded.").

In its paragraph IV notice letter, Nycomed included a statement that the information it contained is confidential and "should not be attached to any complaint or publicly available document." This statement, you argue, constituted an offer of confidential access under § 505(j)(5)(C)(i)(III). Furthermore, your letter asserts that Graceway's review of the notice letter, failure to refuse or object to the confidentiality terms, and subsequent use of the information, constituted acceptance of the offer of confidential access. Nycomed, therefore, argues that § 505(j)(5)(C)(i)(III) applies and preserves the confidential nature of the information contained in its paragraph IV notice letter.[10]

For the reasons stated above, we disagree that Nycomed invoked § 505(j)(5)(C)(i)(III). That section provides a detailed process by which an NDA sponsor or patent owner may obtain access to the ANDA, but it does not contemplate the type of "collapsed" unilateral disclosure that Nycomed used here. The confidential access provision of the Act clearly requires that an offer be made and that "[a] request for access shall be considered acceptance of the offer of confidential access." § 505(j)(5)(C)(i)(III). Notably, the statute does *not* indicate that use of information provided in a paragraph IV notice letter or failure to object to the proposed terms of confidentiality contained in a paragraph IV notice letter constitutes acceptance of such terms. Graceway never requested access to Nycomed's ANDA and, therefore, its review or use of the information in the notice letter does not constitute an acceptance of an offer of confidential access under the plain terms of the statute.

[10] Nycomed's citation to *Biovail Labs, Inc. v. Anchen Pharms, Inc.*, 463 F. Supp.2d 1073, 1083 (C.D. Ca. 2006), is unpersuasive. In that case, in contrast to the situation here, the court objected to the disclosure of information contained in an ANDA that was subject to a court-approved protective order. *Id.*

In addition, we further conclude that Nycomed did not trigger the protections of the confidential access provision because its paragraph IV notice letter did not include an offer of access to "*the application that is in the custody of the [ANDA] applicant.*" § 505(j)(5)(C)(i)(III) (emphasis added). You assert that reliance on this language in the confidential access provision promotes form over substance, and that access to the information derived from your ANDA and included in Nycomed's paragraph IV notice letter is equivalent to access to the actual ANDA. Plainly, however, Congress contemplated that the recipient of the offer of confidential access be able to review "the application" and that that application be "in the custody of the [ANDA] applicant." *Id.* Given this language, it is clear that Congress did not contemplate extending the protections detailed in the confidential access provision to information disclosed in a piecemeal fashion outside the framework provided by that provision, as Nycomed did in its paragraph IV notice letter. In short, reproducing the formulation of Nycomed's product in a paragraph IV notice letter is not equivalent to providing access to the ANDA itself. Indeed, the confidential access provision *expressly establishes* a process where an offer is made in the paragraph IV notice letter, the recipient of the letter takes action to request access, thereby accepting the offer, and the recipient then reviews the actual ANDA held by the applicant. Thus, the confidential access provision is intended to protect the confidentiality of information contained in an ANDA, and not to protect information contained in a paragraph IV notice letter. Under its plain terms, the confidential access provision does not apply here. Accordingly, we conclude that Graceway was not prohibited from further disclosing the alleged trade secrets and confidential commercial information disclosed by Nycomed to Graceway in its paragraph IV notice letter.

C. Section 301(j) of the Act Does Not Prohibit Graceway or FDA From Disclosing Nycomed's Paragraph IV Notice Letter

In addition, you assert that § 301(j) prohibited Graceway from including a copy of Nycomed's paragraph IV notice letter in the Citizen Petition it submitted to FDA. Your argument focuses on the language in § 301(j) that the "using [of certain information] by *any* person to his own advantage..." is prohibited (emphasis added), as evidence that Congress intended for § 301(j)'s prohibition to apply broadly to private entities and government employees and officers alike. As such, you assert that § 301(j) prohibits not just FDA, but also private entities such as Graceway, from disclosing certain trade secrets.

We disagree. As a preliminary matter, as discussed above, because the notice letter was shared by Nycomed with Graceway, neither the letter nor the information in it is considered confidential,[11] and therefore the plain terms of § 301(j) do not apply to the document.

Furthermore, when § 301(j) is considered in the context of the statutory generic drug approval scheme created by Congress, it is clear that § 301(j) cannot apply to NDA sponsors that, like Graceway, have received paragraph IV notification letters pursuant to § 505(j)(2)(B)(ii). We must read "the words of a statute...in their context and with a view to their place in the overall

[11] As explained above, Nycomed did not provide its paragraph IV notice letter to Graceway in a manner which protected its confidentiality and accordingly, to the extent that the information in the paragraph IV notice letter could have been considered a trade secret, Nycomed lost any protections provided to such information under the Act, FOIA, the Trade Secrets Act, and FDA's regulations.

statutory scheme." *FDA v. Brown & Williamson*, 529 U.S. 120, 133 (2000). As explained above, the paragraph IV notice letter is intended "to alert [the NDA sponsor or patent owner] to the possibility of infringement by the ANDA applicant so that the patentee can protect its interest by inquiry, investigation, or litigation." *See, e.g., AstraZeneca AB v. Mutual Pharmaceutical Co., Inc.*, 221 F. Supp.2d 528, 534 (E.D. Pa. 2002). In addition, if certain conditions outlined in § 505(j)(5)(C)(i)(III) are met, an NDA sponsor or patent owner may use information contained in an ANDA "for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of [a paragraph IV certification]." The Act clearly contemplates that NDA sponsors and patent owners may use the information obtained under §§ 505(j)(2)(B) and 505(j)(5)(C) to pursue legal action against the ANDA applicant for patent infringement. § 505(j)(5)(B)(iii).

Section 301(j), if applied in the manner proposed by Nycomed, would prohibit NDA sponsors or patent owners from using the information provided in accordance with 505(j)(2)(B) and 505(j)(5)(C) to pursue legal remedies for potential patent infringement as contemplated by the Act, because the NDA sponsor or patent owner would be "using [the information] to his own advantage." Such an interpretation would render these provisions meaningless. For this reason, too, Nycomed's proposed interpretation must be rejected. *See, e.g.*, 2A Norman J. Singer & J.D. Shamble Singer, *Statutes and Statutory Construction* § 46:6 (7th ed. 2007) (it is a well-accepted canon of statutory construction that a statute should be read so that effect is given to all of its provisions, so that no part will be inoperative or superfluous, void or insignificant).

Therefore, in light of fact that paragraph IV notice letters are inherently public disclosures, FDA concludes that § 301(j) is inapplicable to the information contained in them. We further conclude that Nycomed's proposed interpretation of § 301(j) is inconsistent with the role that the information in a paragraph IV notice letter plays in the statutory generic drug approval scheme. Thus, § 301(j) does not prohibit the disclosure of either paragraph IV notice letters or the information contained in them by NDA holders or patent owners such as Graceway who receive them in the normal course.[12]

D. FDA's Disclosure of the Paragraph IV Notice Letter is Not Inconsistent with Previous Statements Regarding Confidentiality of ANDAs

Our conclusion that Nycomed's paragraph IV notice letter is not confidential is not, as Nycomed argues, inconsistent with the Agency's past statements that it will maintain the confidentiality of an ANDA applicant's identity and the date an ANDA is received. *See* 59 Fed. Reg. 50338, 50354 (Oct. 3, 1994); FDA, Paragraph IV Patent Certifications.[13] Those statements were made in response to requests that the Agency affirmatively disclose non-public information contained

[12] Because we have concluded that the information in a paragraph IV notice letter is not considered confidential and that Nycomed's proposed interpretation of § 301(j) of the Act is inconsistent with the generic drug approval process established in § 505(j), we need not reach the question of whether § 301(j) applies to private entities.

[13] *Available at*: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm047676.htm.

in ANDAs submitted to FDA.[14] Here, by contrast, the Agency has received as an attachment to a citizen petition a copy of a document that was publicly disclosed by an ANDA applicant to its competitor, the NDA sponsor. FDA can acknowledge the existence of an ANDA once the applicant itself has publicly disclosed it (whether by sending a paragraph IV notice letter to the NDA sponsor or patent owner, or by some other means). *See* 21 C.F.R. § 314.430(b).[15] Furthermore, the Agency is not prohibited from accepting (or posting) a citizen petition containing a paragraph IV notice letter, because a paragraph IV notice letter is (as discussed above) a public document.

III. Conclusion

We have considered your October 6, October 26, and December 11, 2009, letters and Graceway's October 16, 2009, and November 18, 2009, letters, as well as the arguments and information presented during meetings the Agency conducted with your client and with Graceway, and relevant statutory and regulatory provisions. For the reasons explained above, disclosure of Nycomed's paragraph IV notice letter to Graceway constituted a disclosure to the public of the information it contained. Therefore, under the Act and FDA's regulations, FDA may not withhold the information from public disclosure. Accordingly, we intend to re-post the Citizen Petition, and its attached exhibits, including Nycomed's paragraph IV notice letter, in the public docket on Wednesday, January 13, 2010, at approximately 5:00 pm.

If you have any questions regarding this matter, please contact Nancy Sager at (301) 796-3603.

Sincerely,

Jane A. Axelrad

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

cc: Michael Landa, Acting Chief Counsel, FDA
Philip Katz, Counsel for Graceway

[14] As explained in its response to two citizen petitions requesting that the Agency include additional information in the "Paragraph IV Patent Certifications" list posted on its website, FDA does not disclose the date a paragraph IV certification was submitted, which may be different than the date the ANDA was submitted, or the identity of the first applicant to submit a substantially complete ANDA containing a paragraph IV certification, because to do so would reveal specific information about an ANDA that is not publicly known. *See* Response to Citizen Petitions 99P-2778 and 00P-1556, at 4 (Feb. 27, 2004).

[15] We note that, although under 21 C.F.R. § 314.430(d)(1), no data or information contained in an application or abbreviated application are available for public disclosure before the agency sends an approval letter, the paragraph IV notice letter as sent to the NDA sponsor or patent owner is not itself contained in the ANDA.

EXHIBIT B

TOLMAR Inc.

April 08, 2010

BY FEDEX OVERNIGHT MAIL

Dr. Ken Cunningham
Chief Executive Officer
SkyePharma PLC
105 Piccadilly
London, UK
W1J 7NJ

Sarah Maxwell
Chief Operating Officer
SkyePharma U.S. Inc.
10450 Science Center Dr
San Diego, CA 92121

Paul McGarty
Chief Executive Officer
Nycomed U.S. Inc.
60 Baylis Road
Melville, NY 11747

Attn: Chief Legal Officer
SkyePharma AG
Eptingerstrasse 51
Muttenz, Switzerland
CH-4132

Michael Kuner
Attn: General Counsel
Nycomed International Management GmbH
Leutschenbachstrasse 95
Zurich, Switzerland
CH-8050

Attn: Chief Legal Officer
SkyePharma US, Inc.
One Broadway
14th floor
Cambridge, MA 02141

Chief Legal Officer
Jagotec AG
Eptingerstrasse 51
Muttenz, Switzerland
CH-4132

Attn: Chief Legal Officer
PharmaDerm
210 Park Avenue
Florham Park, NJ 07932

Re: Notice Of Certification Under 21 U.S.C. § 355(j)(2)(B) (§ 505(j)(2)(B)) Of Federal Food, Drug And Cosmetic Act) And 21 C.F.R. § 314.95
Tolmar, Inc's Diclofenac Sodium, Gel 3%
Tolmar Inc.'s ANDA 20-0936

Dear Sir or Madam:

TOLMAR, Inc. ("TOLMAR"), of 701 Center Avenue, Fort Collins Colorado 80526 hereby gives notice to the NDA holder and/or listed patent owner and marketer, and/or their representatives, for the reference listed drug that the FDA has received an Abbreviated New

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Drug Application ("ANDA") for TOLMAR's gel containing 3.0% Diclofenac sodium ("the TOLMAR GEL"), which contains data or information from required bioequivalence and/or bioavailability studies.

The FDA has assigned to the TOLMAR ANDA the number 20-0936.

By submitting this ANDA, TOLMAR seeks to obtain approval to engage in commercial manufacture, use, sale, offer for sale or import of the TOLMAR GEL prior to the expiration of the following U.S. patents (hereinafter the Solaraze U.S. Patents), which are listed in *Approved Drug Products With Therapeutic Equivalence Evaluation* (the "Orange Book") as having the indicated expiration dates:

U.S. Patent No.	Patent Owner	Patent Expiry
5,639,738	Jagotec, AG/ SkyePharma AG	June 17, 2014
5,792,753	Jagotec, AG/ SkyePharma AG.	August 11, 2015
5,852,002	Jagotec, AG/ SkyePharma AG.	June 17, 2014
5,914,322	Jagotec, AG/ SkyePharma AG	August 11, 2015
5,929,048	Jagotec, AG/ SkyePharma AG	July 27, 2016
5,985,850	Jagotec, AG/ SkyePharma AG	November 16, 2016

The purpose of this communication is to provide the notice and information required by 21 U.S.C. § 355(j)(2)(B)(i) and/or (ii) (Sections 505(j)(2)(B)(i) and/or (ii) of the Food, Drug and Cosmetics Act) and to inform you that the TOLMAR ANDA contains certifications under 21 U.S.C. § 355(j)(2)(A)(vii)(IV), which assert that the claims of said Solaraze U.S. Patents will not be infringed by the manufacture, use, sale, offer for sale or import of the TOLMAR GEL.

A Detailed Statement of the factual and legal basis of TOLMAR's opinion is appended hereto. The detailed statement sets forth TOLMAR's factual and legal basis that the Solaraze U.S. Patents are not infringed by the manufacture, use, sale, offer for sale or import of the TOLMAR GEL.

Offer for Confidential Access

An Offer of Confidential Access to relevant sections of the TOLMAR ANDA pursuant to 21 U.S.C. § 355(j)(5)(C)(i)(III) is attached hereto.

Anticompetitive Behavior Warning

Please be warned of the following. It is an antitrust violation to assert a patent known not to be infringed. *Locitie v. Ultraseal*, 781 F.2nd 861 (Fed.Cir. 1985). As such, the attached Detailed Statement has outlined in the necessary detail that your patents are not, and cannot be, infringed by the subject matter described in the TOLMAR ANDA. As such, your pursuit of an infringement action may be deemed to be an antitrust violation. In addition, it is an antitrust violation to assert a patent known not to be valid. *Handgards v. Ethicon*, 610 F.2n 986 (9th Cir.

1979). If you launch any patent infringement lawsuit, either now or later, TOLMAR may pursue the appropriate remedies against you, including seeking fees, costs and sanctions for potential violations of Rule 11(of the Civil Procedure Rules), exceptional case and frivolous suit statutes under the penalty laws, and for violations of the antitrust laws, plus any remedy the court deems fit to award.

Reservation of Legal Rights

We reserve the right to allege the same, similar, different or new theories of non-infringement and/or invalidity and nothing in this Notice Letter or Detailed Statement shall be construed as to limit our rights to make any allegation in any subsequent litigation regarding any issue.

Relevant Contact Information

If you have any inquiries concerning this notice, please contact Sean F. Moriarty, Vice President General Counsel, TOLMAR at the following address: 701 Center Avenue, Fort Collins, Colorado 80526.

Very truly yours,

Michelle R. Bayer
Regulatory Affairs – TOLMAR, Inc.

Enclosures:
Offer of Confidential Access
Detailed Statement

CC:

John Murphy
General Counsel
SkyePharma PLC
105 Piccadilly
London, W1J7NJ, United Kingdom

EXHIBIT C

TOLMAR Inc.

TOLMAR'S OFFER OF CONFIDENTIAL ACCESS PURSUANT TO 21 U.S.C. § 355 (j)(5)(C)(i)(III)

Pursuant to 21 U.S.C. § 355 (j)(5)(C)(i)(III), and subject to the restrictions detailed below, TOLMAR hereby provides this Offer of Confidential Access ("Offer") to the NDA holder and the Patent owner (hereinafter, each "Company") for the sole purpose of determining whether to bring an action referred to in 21 U.S.C. § 355 (j)(5)(B)(iii) with respect to the Listed Patents.

1. This Offer is subject to the following restrictions as to persons entitled to access and the use and disposition of any information accessed:

A. Persons Entitled to Access: Persons entitled to access ("Authorized Evaluators") under this Offer of Confidential Access are restricted to: (i) no more than two outside counsel engaged by each Company to represent it and the staff of such outside counsel, including paralegal, secretarial and clerical personnel who assist such counsel; and (ii) independent consultants and experts assisting in the evaluation of possible infringement of the Listed Patent and any employees and assistants under the control of such consultant or expert; provided that all such persons contemplated by this paragraph A are identified to TOLMAR in writing and are not involved in the prosecution of any patent(s) related to Diclofenac, salts thereof and/or regulatory approval of a gel containing Diclofenac sodium.

B. Materials Accessible by Authorized Evaluators: A copy of the relevant sections of the ANDA, as determined by TOLMAR, redacted to remove information of no relevance to any issue of patent infringement, will be provided for use by Authorized Evaluators.

C. Use of the ANDA and Information in the ANDA:

(1). The ANDA and all information contained therein or derived therefrom may be used for the sole and limited purpose of evaluating possible infringement of the Listed Patent(s) and for no other purpose.

(2). Authorized Evaluators shall not disclose any information contained in or derived from the ANDA or any notes, analyses, studies or other documents to the extent that they reflect any information in the ANDA, to any person other than persons entitled to access under subsection 1.A.

(3). Notwithstanding the provisions of subsections 1.C.(1) and 1.C.(2) above, Authorized Evaluators shall be permitted to advise the Company whether to bring suit alleging infringement of the Listed Patent(s); provided, however, that the information in the ANDA is not thereby disclosed.

D. Disposition of the Information in the ANDA:

(1). The Company agrees that if it does not file suit against TOLMAR alleging infringement of one or more of the Listed Patents within forty-five (45) days of receipt of the Notice and Detailed Statement (the "45-day period"), which this Offer accompanies, the Company shall cause Authorized Evaluators within thirty (30) days after the expiration of the 45-day period, to destroy or return to TOLMAR all portions of the ANDA provided, and all notes, analyses, studies or other documents to the extent that they contain information in the ANDA, and the Company shall notify TOLMAR in writing within a reasonable time that this has been done.

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(2). The Company agrees that if The Company files suit against TOLMAR alleging infringement of one or more of the Listed Patents within the 45-day period:

(a) While the litigation is pending, the portions of the ANDA provided and all notes, analysis, studies or other documents to the extent that they contain information in the ANDA, shall be treated as information under the highest level of confidentiality under any protective order entered in the action brought against TOLMAR. Until such a protective order is entered, subsections 1.C.(1) and 1.C.(2) above continue to apply.

(b) The Company shall cause Authorized Evaluators to destroy or return to TOLMAR the portions of the ANDA provided and all notes, analyses, studies or other documents prepared to the extent that they contain information in the ANDA, within thirty (30) days after the final determination of the action brought against TOLMAR.

E. Accidental Disclosure: Should information contained in the ANDA be disclosed, inadvertently or otherwise, The Company shall, at its earliest reasonable opportunity, by and through Authorized Evaluators, contact TOLMAR and identify:

(1) what has been disclosed;
(2) the individuals to whom such information has been disclosed; and
(3) steps taken by The Company and Authorized Evaluators to ensure the information in the ANDA is not further disseminated.

2. The Company acknowledges that the violation of any provision of this Offer will cause irreparable injury to TOLMAR, and that an adequate legal remedy does not exist. TOLMAR, therefore, shall have the right, in addition to any other remedies available at law or in equity, to obtain from a court of competent jurisdiction an injunction to prohibit The Company from violating the terms of this Offer. The Company agrees that in such an action TOLMAR is entitled to recover any and all damages, costs and expenses, including, but not limited to, all reasonable attorneys' fees, professional fees and court costs.

3. Should any provision set forth in this Offer be found by a court of competent jurisdiction to be illegal, unconstitutional or unenforceable, the remaining provisions shall continue in full force and effect.

4. Nothing contained herein shall be construed as a grant of any license or other right to use the information in the ANDA except for the purpose expressly stated herein.

5. When accepted by The Company, this document shall constitute the entire agreement of the parties with respect to the subject matter herein and may not be amended or modified except in writing executed by the parties.

6. The Company may request access to the ANDA by executing one copy of this Offer where indicated and returning the executed copy, within a reasonable time before the expiration of the 45-day period, to Sean F. Moriarty, TOLMAR Inc., 701 Centre Avenue, Fort Collins, CO 80526. Thereupon, the terms contained in this document shall be considered an enforceable contract between TOLMAR and The Company.

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7. The Company agrees that any claims for breach of this Agreement may be brought in courts located in the State of Colorado and consents to the jurisdiction and venue of such courts for any such claims.

TOLMAR INC.
By its authorized agent:

Sean F. Moriarty
Vice President General Counsel

ACCEPTED AND AGREED:

SkyePharma U.S. Inc.
By its authorized agent:

Signature:_____

Name (Print):_____

Title:_____

Company:_____

Date:_____

Nycomed U.S. Inc.
By its authorized agent:

Signature:_____

Name (Print):_____

Title:_____

Company:_____

Date:_____

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CONFIDENTIAL

TOLMAR INC.'S DETAILED STATEMENT OF THE FACTUAL AND LEGAL BASES FOR ITS OPINION THAT U.S. PATENT NO(S) 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, and 5,985,850 ARE INVALID, UNENFORCEABLE AND/OR ARE NOT INFRINGED BY THE MANUFACTURE, USE, IMPORTATION, SALE OR OFFER FOR SALE OF THE TOLMAR GEL.

TOLMAR Inc. ("TOLMAR") has requested United States Food and Drug Administration approval of its Diclofenac sodium gel. 3.0% ("the TOLMAR GEL") under ANDA No. 200936. In making this request, TOLMAR seeks approval of the commercial manufacture, use, sale, offer for sale and import of the TOLMAR GEL prior to the expiration of U.S. Patent No's. 5,639,738; 5,792,753; 5,852,002; 5,914,322; 5,929,048 and 5,985,850 ("the '738, '753, '002, '322, '048 and '850 patents" or "Solaraze patents" as a group).

Accordingly, TOLMAR sets forth this Detailed Statement pursuant to 21 U.S.C. § 355(j)(2)(B)(i) and (ii), to provide the factual and legal basis for TOLMAR's opinion that the Solaraze patents are not infringed by the manufacture, use, sale, offer for sale or import of the TOLMAR GEL. Because additional defenses to patent infringement may occur, be developed, be uncovered and/or be discovered in the future, if sued for patent infringement, TOLMAR expressly reserves the right to assert additional related and unrelated defenses to patent infringement in addition to those set forth below. These defenses include, but are not limited to, non-infringement, invalidity and unenforceability, or any other claim construction as to the Listed Patents in the event of litigation.

This detailed statement is hereby incorporated by reference into the Notice to which it is appended.

Further, please be advised that TOLMAR considers this information to be confidential, is disclosing this information solely to comply with 21 U.S.C. §355(j)(2)(B), and requests that the recipients protect this information from disclosure to third parties by means consistent with their own standards for protecting their own confidential information. THIS CONFIDENTIALITY APPLIES TO THIS STATEMENT, WHICH MAY NOT, AND SHOULD NOT, BE ATTACHED TO ANY COMPLAINT OR OTHER PUBLICLY AVAILABLE DOCUMENT.

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FACTUAL AND LEGAL BASIS FOR NON-INFRINGEMENT

TOLMAR AND THE TOLMAR GEL

TOLMAR Inc., a Delaware corporation, wishes to obtain approval to market the TOLMAR GEL and has filed a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) asserting that the claims of the Solaraze patents will not be infringed by the manufacture, use, sale, offer for sale or import of the TOLMAR GEL.

The TOLMAR GEL includes Diclofenac sodium (3 wt %), polyethylene glycol monomethyl ether, benzyl alcohol, PEG-60 hydrogenated castor oil, hydroxyethyl cellulose and purified water.

APPLICABLE LAW

A. Non-Infringement

The first step in the assessment of patent infringement is to construe the claim terms, which is a matter of law for the court. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (*en banc*), *aff'd*, 116 S.Ct. 1384 (1996). Whether a product infringes a claim requires a two-step analysis. First, the claims must be interpreted. Second, the properly-interpreted claims must be compared to the accused product. *Markman*, 116 S. Ct. at 1393; *Texas Instruments, Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558 (Fed. Cir. 1996). To literally infringe a claim, the accused product must practice every limitation in the claim. *Texas Instrum.*, 90 F.3d at 1563.

A product may infringe a patent under the doctrine of equivalents if it contains elements equivalent to each claimed element of the patented invention. Depending upon the facts of a given case, such element-by-element equivalency may be established by proof of insubstantial differences in the role played by elements of the claim and the accused product, or by proof that an accused element performs substantially the same function, in substantially the same way, to produce substantially the same result as the claimed element of the patented invention. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17 (1997); see also *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605 (1950). The differences are to be assessed by an element-by-element approach. If an element is entirely missing from the accused composition or method, and no equivalent is present, the accused composition or method cannot be infringing under the

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doctrine of equivalents. *Hilton Davis*, cited *supra*.

The doctrine of equivalents is also subject to the ancillary doctrine of prosecution history estoppel, which acts to limit infringement by otherwise equivalent products or processes. *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211 (Fed. Cir. 1995).

Furthermore, the doctrine of equivalents is constrained by the prior art. *Wilson Sporting Goods Co. v. David Geoffrey & Assoc.*, 904 F.2d 677 (Fed. Cir. 1990). The doctrine does not permit a patent claim to encompass subject matter that could not have been patented. *Id.* ("[A] patentee should not be able to obtain, under the doctrine of equivalents, coverage which he could not lawfully have obtained from the PTO by literal claims."); see also *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570 (Fed. Cir. 1995) (the doctrine of equivalents does not permit coverage of obvious or "trivial" variations of the prior art).

U.S. Patent No. 5,639,738

U.S. Patent No. 5,639,738, filed on February 21, 1992, issued on June 17, 1997 and is listed in the Orange Book as expiring on June 17, 2014. The '738 patent issued with eighteen claims. Claims 1, 7 and 11 are independent and are illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

> **1. A method of treating a mammal for a condition of the skin or exposed tissue selected from the group consisting of basal cell carcinoma and actinic keratosis, which method consists essentially of topically administering to the site of the condition, more than once per day over a period of days sufficient to treat the condition, a non-toxic effective dosage amount of a composition consisting essentially of**
>
> **(a) a non-steroidal anti-inflammatory drug (NSAID) in an amount sufficient to block prostaglandin synthesis,**
>
> **(b) hyaluronic acid or a pharmaceutically acceptable salt thereof in an amount effective to transport said NSAID into the skin or exposed tissue at the site of the condition, wherein the concentration of the hyaluronic acid or salt thereof is between 1–3% by weight of the composition, and the molecular weight of the hyaluronic acid or salt thereof is between 150,000 and 750,000 Daltons, and**

(c) a pharmaceutical excipient suitable for topical application.

7. A method of treating a mammal for a condition of the skin or exposed tissue selected from the group consisting of basal cell carcinoma and actinic keratosis, which method consists essentially of topically administering to the site of the condition, more than once per day over a period of days sufficient to treat the condition, a non-toxic effective dosage amount of a composition consisting essentially of

(a) a non-steroidal anti-inflammatory drug (NSAID) in an amount sufficient to block prostaglandin synthesis, wherein the concentration of the NSAID between 1–5% by weight of the composition,

(b) hyaluronic acid or a pharmaceutically acceptable salt thereof in an amount effective to transport said NSAID into the skin or exposed tissue at the site of the condition, wherein the concentration of the hyaluronic acid or salt thereof is between 1–3% by weight of the composition, and the molecular weight of the hyaluronic acid or salt thereof is between 150,000 and 750,000 Daltons, and

(c) a pharmaceutical excipient suitable for topical application.

11. A method of treating a mammal for actinic keratosis of the skin or exposed tissue, which method consists essentially of topically administering to the site of the actinic keratosis, more than once per day over a period of days sufficient to treat the actinic keratosis, a non-toxic effective dosage amount of a composition consisting essentially of

(a) a non-steroidal anti-inflammatory drug (NSAID) in an amount sufficient to block prostaglandin synthesis;

(b) hyaluronic acid or a pharmaceutically acceptable salt thereof in an amount effective to transport said NSAID into the skin or exposed tissue at the site of the actinic keratosis, wherein the concentration of the hyaluronic acid or salt thereof is between 1–3% by weight of the composition, and the molecular weight of the hyaluronic acid or salt thereof is between 150,000 and 750,000 Daltons, and

(c) a pharmaceutical excipient suitable for topical application.

U.S. Patent No. 5,792,753

U.S. Patent No. 5,792,753 ,filed on February 17, 1993, issued on August 11, 1998 and is listed in the Orange Book as expiring on August 11, 2015. The '753 patent issued with sixteen claims.

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Claim 1 is the only independent claim and is illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

> **1. A topically administrable pharmaceutical composition comprising a therapeutically effective amount of a drug which inhibits prostaglandin synthesis, and an amount of a form of hyaluronic acid sufficient to transport the composition through the skin into the epidermis or dermis where the composition remains until discharged via the lymphatic system, wherein**
>
> **(a) the drug is 1–5% by weight of the composition, and**
>
> **(b) the form of hyaluronic acid is 1–3% by weight of the composition, has a molecular weight greater than about 150,000 daltons and less than 750,000 daltons, and is selected from the group consisting of hyaluronic acid and salts thereof.**

U.S. Patent No. 5,852,002

U.S. Patent No. 5,852,002, filed on June 5, 1995, issued on December 22, 1998 and is listed in the Orange Book as expiring on June 17, 2014. The '002 patent issued with eleven claims. Claims 1-2, 4-6, 8 and 10 are independent and are illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

> **1.** A method of treating a condition or disease in a human involving tissue selected from the group consisting of underperfused tissue and pathological tissue which will benefit from the treatment by the administration of an agent selected from the group consisting of a medicinal agent and a therapeutic agent and combinations thereof, which is suitable for treating said tissue, the method comprising administering to the human a therapeutically effective dosage amount of a pharmaceutical composition comprising a therapeutically effective amount of the agent to treat the disease or condition involving tissue selected from the group consisting of underperfused tissue and pathological tissue, and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-

toxic salts and combinations thereof sufficient to facilitate the transport and penetration of the agent through the tissue at a site to be treated through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 3000 mg.

2. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating infection involving underperfused tissue and pathological tissue in humans, said dosage amount comprising a therapeutically effective amount of an agent selected from the group consisting of antibiotics, antibacterials, antimicrobials and combinations thereof with or without ascorbic acid and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg.

4. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating infections surrounding implants involving underperfused tissue and pathological tissue in a patient, said dosage amount comprising a therapeutically effective amount of an antibiotic agent for treating the infected tissue surrounding the implant and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport and penetration of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg. and less than 3000 mg.

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5. A method of treating infection involving underperfused tissue and pathological tissue in humans, the method comprising the administration of a therapeutically effective amount of an agent selected from the group consisting of antibiotics, antibacterials, antimicrobials and combinations thereof with or without ascorbic acid and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport and penetration of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 3000 mg.

6. A method of treating infections surrounding implants involving underperfused tissue and pathological tissue in a patient, the method comprising the administration of a therapeutically effective amount of an antibiotic for the infected tissue surrounding the implant and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport and penetration of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 3000 mg.

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8. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for the prevention of topical infection involving underperfused tissue and pathological tissue in humans, said dosage amount comprising an effective amount of an anti-metabolite agent for preventing topical infection and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport and penetration of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 3000 mg.

10. A method of (preventing) treating a topical infection resulting from a condition or disease in a human involving underperfused tissue and pathological tissue in humans, the method comprising the administration of an effective amount of an anti-metabolite agent and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof to facilitate the transport and penetration of the agent at a site to be treated by the agents passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 3000 mg.

U.S. Patent No. 5,914,322

U.S. Patent No. 5,914,322,,filed on June 6, 1995, issued on June 22, 1999 and is listed in the Orange Book as expiring on August 11, 2015. The '322 patent issued with five claims. Claim 1 is independent and is illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

1. A topically applied transdermally penetrating systemic independent acting pharmaceutical formulation for the treatment of a disease or condition of the skin and exposed tissue said disease or condition being selected from the group consisting of basal cell carcinoma, the precancerous, often recurrent, actinic keratoses lesions, fungal lesions, "liver" spots, lesions (found for the most part in the epidermis), squamous cell tumours, metastatic cancer of the breast to the skin, primary and metastatic melanoma in the skin, genital warts, cervical cancer, and HPV (Human Papilloma Virus), psoriasis (both plaque-type psoriasis and nail bed psoriasis), corns on the feet and hair loss on the head of pregnant women, said formulation comprising, together with pharmaceutical excipients suitable for topical application, a therapeutically effective non-toxic amount of a drug which inhibits prostaglandin synthesis administered with, or carried in, an amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof sufficient to facilitate the drug's penetration through the skin and tissue at a site requiring treatment, to block prostaglandin synthesis, wherein the molecular weight of the form of hyaluronic acid is less than 750,000 daltons and greater than 150,000 daltons and wherein the form of hyaluronic acid is present in an amount between about 1% and about 3% by weight, and wherein the drug is present in an amount between about 1% and about 5% by weight of the formulation.

U.S. Patent No. 5,929,048

U.S. Patent No. 5,929,048, filed on June 5, 1995, issued on July 27, 1999 and is listed in the Orange Book as expiring on July 27, 2016. The '048 patent includes seven claims. Claims 1-2 and 5 are independent and are illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

1. A method of treating a condition or disease in a human involving tissue selected from the group consisting of underperfused tissue and pathological tissue which will benefit from the treatment by the administration of an agent selected from the group consisting of a medicinal agent and a therapeutic agent and combinations thereof, which is suitable for treating said tissue, the method comprising administering to the human a therapeutically effective dosage amount of a pharmaceutical composition comprising a therapeutically effective amount of the agent to treat the disease or condition involving tissue selected from the group consisting of underperfused tissue and pathological tissue, and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof sufficient to facilitate the transport and penetration of the agent through the tissue at a site to be treated through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg.

2. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating a disease and condition involving underperfused tissue and pathological tissue in humans selected from the group consisting of renal failure, cardiac insufficiency, hypertension and edema, said dosage amount comprising an effective amount of a diuretic agent for treating said disease and condition, and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts and combinations thereof sufficient to facilitate the transport of the agent at a site to be treated by the agent passing through the tissue through the cell membranes into the individual cells to be treated wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 1000 mg.

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5. A method of treating a disease or condition involving underperfused tissue and pathological tissue in humans, said disease or condition selected from the group consisting of renal failure, cardiac insufficiency, hypertension and edema, the method comprising the administration of an effective amount of a diuretic agent for treating said disease or condition, and a sufficient amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and its non-toxic salts thereof and combinations thereof to facilitate the transport of the agent at a site to be treated by the agent passing through the tissue through the cell membranes into the individual cells to be treated, wherein the molecular weight of the form of hyaluronic acid is in the range of 150,000 to 750,000 daltons, and said amount of the form of hyaluronic acid is sufficient to provide a dosage greater than 10 mg and less than 1000 mg.

U.S. Patent No. 5,985,850

U.S. Patent No. 5,985,850, filed on June 5, 1995, issued on November 16, 1999 and is listed in the Orange Book as expiring on November 16, 2016. The '048 patent includes ninety-two claims. Claims 1, 42, 44, 83-84 and 92 are independent and are illustrated below. A copy of this patent can be obtained from the U.S. Patent and Trademark Office web site (www.uspto.gov).

1. A dosage amount of a pharmaceutical composition containing a suitable pharmaceutically acceptable excipient comprising:

(1) a therapeutically effective amount of an agent to treat a disease or condition involving underperfused tissue and pathological tissue in humans;

and (2) a form of hyaluronic acid selected from the group consisting of hyaluronic acid and pharmaceutically acceptable salts thereof and combinations thereof

characterized in that said dosage amount of said composition

(a) is in a dosage form which is suitable for administration in humans;

and (b) is in a form in which (i) component (1) is in an effective dosage amount to treat said disease or condition involving underperfused tissue and pathological tissue by penetration at the site to be treated; and (ii) component (2) is available to transport component (1) from the point of administration to the site to be treated, and which component (2) is in an effective non-toxic amount to facilitate the transport of component (1) upon administration from the site of administration to the site in need of treatment, through the tissue, at the site to be treated and through cell membranes into individual cells to be treated, wherein said amount of component (2) is sufficient to provide a dosage of 10 mg to 3000 mg of component (2) and wherein the molecular weight of component (2) is less than 750,000 daltons and greater than 150,000 daltons.

42. A dosage amount of a pharmaceutical composition for treating a condition or disease involving underperfused or pathological tissue comprising a therapeutically useful agent to a patient, the improvement which comprises additionally an amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid and combinations thereof, wherein the amount is between 10 mg and 3000 mg and is sufficient to facilitate passage of the agent and the form of hyaluronic acid to the underperfused or pathological tissue, and wherein the molecular weight of the form of hyaluronic acid is less than 750,000 daltons but greater than 150,000 daltons.

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83. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient therefor comprising an agent selected from the group consisting of a medicinal agent and a therapeutic agent and combinations thereof, and a form of hyaluronic acid, the improvement comprising that the dosage amount of the composition is suitable for treating a condition or disease involving tissue selected from the group consisting of underperfused tissues and pathological tissue in a human, wherein a therapeutically effective amount of the agent is provided in combination with an effective amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof and combinations thereof sufficient to facilitate transportation of the agent to the site to be treated through the tissue and cell membranes into individual cells to be treated, wherein said amount of the form of hyaluronic acid is present in an amount of between 10 mg and 1000 mg of the form of hyaluronic acid, and wherein the molecular weight of the form of hyaluronic acid is less than 750,000 daltons and greater than 150,000 daltons.

84. A dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient therefor for treating a disease or condition involving tissue selected from the group consisting of underperfused and pathological tissue in a human comprising an effective amount of an agent selected from the group consisting of a free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-inflammatory drugs (NSAIDS), steroidal anti-inflammatory drugs, anti-fungal agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia monoclonal antibody, diuretics, immunosuppressants, lymphokines, α and β interferon, insulin, estrogen, progestogen, anti-metabolites, calcium channel blockers, drugs for the treatment of psoriasis and combinations thereof and an effective amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof and combinations thereof sufficient to facilitate

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the agent's penetration through tissue including scar tissue, at site to be treated, through cell membranes into individual cells to be treated, wherein said amount of the form of hyaluronic acid is sufficient to provide a dosage between 10 mg and 1000 mg of the form of hyaluronic acid and wherein the molecular weight of the form of hyaluronic acid is less than 750,000 daltons and greater than 150,000 daltons, with the proviso that if the agent selected is phloretin, it is solubilized.

92. A dosage of a pharmaceutical composition comprising an effective amount of an agent selected from the group consisting of phloridzin, phloretin, and 5-deoxyglucuronide of phloridzin; Vitamin C; and a non-steroidal anti-inflammatory drug, and combinations thereof to competitively block glucose transport in neoplastic cells and an amount of a form of hyaluronic acid selected from the group consisting of hyaluronic acid and pharmaceutically acceptable salts thereof and combinations thereof sufficient to facilitate the agent's penetration through tissue at a site to be treated, through cell membranes into individual cells to be treated and where phloretin is the selected agent, it is solubilized by a solubilizing agent, wherein said amount of the form of hyaluronic acid is sufficient to provide a dosage of 10 mg to 1000 mg of the form of hyaluronic acid and wherein the molecular weight of the form of hyaluronic acid is less than 750,000 daltons and greater than 150,000 daltons.

The TOLMAR GEL Does Not Infringe Any Claim Of The Solaraze Patents

As set forth above, every claim in each of the '738, '753, '002, '322, '048 and '850 patents requires, *inter alia*, the presence of or use of a form of hyaluronic acid or a salt thereof. The TOLMAR GEL does not contain hyaluronic acid in any form or any salt thereof, and does not employ hyaluronic acid or a salt thereof in any concentration or at any molecular weight.

The TOLMAR GEL Does Not Literally Infringe Any Claim Of The Solaraze Patents Because The TOLMAR GEL Does Not Contain Hyaluronic Acid In Any Form Or Any Salt Thereof.

Every independent claim of the Solaraze patents requires the presence of hyaluronic acid or a salt of hyaluronic acid. Thus, an accused composition or an accused method must therefore include hyaluronic acid or a salt of hyaluronic acid in order to find literal infringement of the

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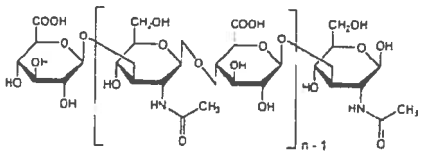
claims of the Solaraze patents.

The term *hyaluronic acid* refers to an unbranched high molecular weight polysaccharide made up of alternating glucuronic acid and N-acetyl glucosamine units. Hyaluronic acid is present in the connective tissue of all vertebrates as the hyaluronate; in man high concentrations are found in skin, cartilage, in the umbilical cord, in vitreous body and in synovial fluid. Hyaluronic acid has the CAS Registry Number [9004-61-9], and the chemical structure shown below:

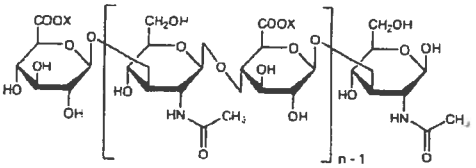


Hyaluronic Acid

Formula I

See Merck Index (14th ed.) at entry 4757, pages 822-823.

Hyaluronic acid includes multiple carboxylic acids, each one in the protonated (*i.e.*, COOH) form, or in the salt (*i.e.*, COOX, wherein X is a suitable counter ion) form. As such, a "*a salt*" of hyaluronic acid refers to the compound shown below:



Salts of hyaluronic acid wherein X is a suitable counter ion.

Formula II

Suitable counter ions, X, that give rise to salts include, *e.g.*, sodium (Na^+), potassium (K^+) and calcium (Ca^+). In addition, *Pharmaceutical Salts*, Stephen M. Berge, Lyle D. Bighley and

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Donald C. Monkhouse, Journal of Pharmaceutical Sciences, Vol. 66, No. 1, pp. 1-19 (1977) at Table I provides for seven organic and seven metallic (*i.e.*, total of fourteen) FDA-approved, commercially marketed cations that are useful for making pharmaceutically acceptable salts. These cations include the organic cations: benzathine, chloroprocaine, choline, diethenolamine, ethylenediamine, meglumine and procaine; as well as the metallic cations: aluminum, calcium, lithium, magnesium, potassium, sodium and zinc.

The Solaraze patentees used the term term *hyaluronic acid or a salt thereof* in a manner that is consistent with the plain meaning described above. In doing so, the patentees stated, for example:

> Hyaluronic acid is a naturally occurring glycosaminoglycan. Its molecular weight may vary from 50,000 dalton upwards, and it forms highly viscous solutions. As regards the actual molecular weight of hyaluronic acid in natural biological contexts, this is still a matter of much uncertainty; when the molecular weight of hyaluronic acid is to be determined, different values are obtained depending on the assay method employed, and on the source, the isolation method etc. The acid occurs in animal tissue, e.g. spinal fluid, ocular fluid, synovial fluid, cockscombs, skin, and also in some streptococci. Various grades of hyaluronic acid have been obtained. A preparation with an allegedly high degree of purity and alleged to be entirely free from side effects is a non-inflammatory form described in U.S. Pat. No. 4,141,973; this preparation is said to have a molecular weight exceeding 750,000 dalton, preferably exceeding 1,200,000 dalton and is suggested for therapeutic use in various articular conditions

See '738 patent at column 1, line 56- col. 2, line 6 and the corresponding text of the other Solaraze patents, for example, the '048 patent at col. 4, lines 28-45 .

The Solaraze patentees also explained this term during the prosecution of those patents. At various times during these prosecutions, they made the following statements.

> Applicants have amended the forms of hyaluronic acid in the claims to hyaluronic acid and its non-toxic salts. The term 'salts' does not encompass a large number of components and, in fact, would be readily understood by a person skilled in the art. The salts are referring to salts of hyaluronic acid.

See, e.g., page 14 of the Amendment and Response (A&R) of the '850 patent prosecution dated

December 25, 1996.

> Applicants have removed the terms 'homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid', and have limited the molecular weight of the form of hyaluronic acid to the range of 150,000 to 750,000 daltons, overcoming the 35 U.S.C... §112, first paragraph rejection.

See page 15 of the Amendment and Response (A&R) of the '850 patent prosecution dated December 25, 1996. It follows that the term *hyaluronic acid or a salt thereof* means a compound of Formulas I and/or II shown on the foregoing pages.

The TOLMAR GEL and the method for its administration to topically treat actinic keratoses do not include hyaluronic acid, or a salt of hyaluronic acid. No ingredient present in the TOLMAR GEL is a hyaluronic acid or its salt. In other words, the TOLMAR GEL does not contain a compound of Formulas I and/or II shown on the foregoing pages. Accordingly, for at least these reasons, the TOLMAR GEL, and the method for administration of the TOLMAR GEL to topically treat actinic keratoses (AK), do not literally infringe any claim of U.S. Patent Nos. 5,639,738, 5,792,753, 5,852,002, 5,914,322, 5,929,048, or 5,985,850.

The TOLMAR GEL Does Not Infringe Any Claim Of The Solaraze Patents Under The Doctrine Of Equivalents

During the prosecution of the Solaraze patents, the patentees distinguished the compositions recited therein from the prior art compositions and in response to rejections under 35 U.S.C. § 112. In doing so, the patentees created a prosecution history that established an estoppel against interpretation of the claims of all Solaraze patents as excluding the compound hyaluronic acid, and salts of hyaluronic acid. In particular, the patentees repeatedly explained that the minimum dosage and molecular weight of their hyaluronic acid or salt thereof distinguished their claimed composition from prior art which also disclosed use of hyaluronic acid. The patentees explained their composition parameters enhanced the performance of the recited drug. For example, the Solaraze patentees said that:

> The minimum dosage amount and the specific molecular weight

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> of hyaluronic acid disclosed and claimed in applicant's application enhances the performance of the drug in the human body and produces the unusual targeting of the conditions and the diseases involving underperfused tissue and the pathological tissue, as would be understood by persons skilled in the art.

See page 19 of the '850 Amendment and Response (A&R) dated January 3, 1998.

> There is no teaching whatsoever of the use of a form of hyaluronic acid which (a) facilitates penetration, (b) has a molecular weight in the range of 150,000 to 750,000 daltons, and (c) provides a dosage greater than 10mg/70kg person.

See page 23 of the '002 Amendment and Response (A&R) dated December 24, 1996.

In concert with these comments, the Solaraze patentees amended the claims of the Solaraze patents by narrowing those claims to recite only hyaluronic acid or salt thereof having certain molecular weight and dosage limitations. Their amendments also eliminated claim recitations of "analogues, derivatives, complexes, esters, fragments and subunits" of hyaluronic acid or a salt thereof. Hence, the patentees moved from a broader definitional scope of hyaluronic acid, analogs, derivatives and the like to a very narrow scope of only hyaluronic acid.

Therefore, the prosecution histories of the Solaraze patents establish a prosecution history estoppel. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 122 S. Ct. 1831 (2002)(a narrowing amendment made to satisfy any requirement of the Patent Act gives rise to estoppel). As set forth above, the amendments to the Solaraze patents claims to recite only the term *hyaluronic acid or a salt thereof* and eliminated analogs, derivatives and the like of hyaluronic acid, which means that equivalents of this term do not even reach to analogs and derivatives of hyaluronic acid. It follows that because the term *hyaluronic acid* has this extremely narrow scope, it clearly does not extend under the doctrine of equivalents to compounds that are structurally unrelated. This prosecution history estoppel, accordingly, precludes the Solaraze patentees from asserting that any inactive ingredient of the TOLMAR GEL is the equivalent of hyaluronic acid or a salt of hyaluronic acid.

In *Festo*, the Supreme Court ruled that there is a rebuttable presumption that a patentee who narrows a claim by amendment to avoid a prior art rejection, surrenders all the territory

between the original claim breadth and the narrowed claim elements. The patentee can rebut the presumption by explaining that (1) the equivalent was unforeseeable at the time of the application; (2) the rationale underlying the amendment bears no more than a tangential relation to the equivalent in question; or (3) some other reason exists suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question.

Here, the Solaraze patentees cannot meet this burden to rebut the presumption. The TOLMAR GEL contains diclofenac sodium and common and ordinary excipients for topical formulations such as creams and lotions, which were available at the time of the patent applications filings. Hence, the Solaraze patentees are precluded from asserting that use of any of these TOLMAR GEL ingredients as excipients for topical formulations was unforeseeable when the Solaraze patents were filed or that the Solaraze patentees could not have described the TOLMAR GEL common and ordinary excipients in the patents claims. Additionally, the rationale underlying the amendments of the Solaraze patents claims were not tangential to the equivalent in question. For example, during prosecution of the '048 application, the patentees distinguished the Lowry reference, which according to the patentee disclosed propylene glycol as opposed to hyaluronic acid as a penetrating agent. *See* August 4, 1997 Response to Office Action, pp. 15-16. Thus, the Solaraze patentees cannot now assert that other excipients are tangential to the amended limitations requiring hyaluronic acid or salts thereof.

Therefore, the Solaraze patent claims cannot be interpreted under the doctrine of equivalents to cover formulations or their use that do not include *hyaluronic acid or a salt thereof.*

The Federal Circuit has held that even if no claim amendments were made during prosecution, both disclosing and claiming an invention narrowly can preclude access to the doctrine of equivalents. The Federal Circuit stated:

> Thus for a patentee who has claimed an invention narrowly, there may not be infringement under the doctrine of equivalents in many cases, even though the patentee might have been able to claim more broadly... [citing *Maxwell v. Baker*, with approval as] discussing the danger of allowing patentee to file and prosecute narrow claims and then, during the course of litigation, to expand its exclusive rights under the doctrine of equivalents thereby

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avoiding examination of broader subject matter.

See Sage Prods. v. Devon Indust., 126 F.3d 1420 (Fed. Cir. 1997). *See also North American Vaccine v. American Cyanamid*, 7 F.3d 1571; 28 U.S.P.Q.2d 1333, 1337 (Fed Cir 1993), which stated:

> A patentee cannot disclose and claim an invention narrowly and then, in the course of an infringement suit, argue effectively that the claims should be construed to cover that which is neither described nor enabled in the patent.

Likewise, the claims cannot be argued narrowly during prosecution and then broadly, to entrap accused infringers. *See Southwall Technologies, Inc. v. Cardinal IG Co.*, 54 F.3d 1570 (Fed. Cir. 1995).

The Solaraze patentees disclosed and claimed each of the respective inventions with the narrow term *hyaluronic acid or a salt thereof.* Pursuant to *Sage Products v. Devon Indus.*, 126 F.3d 1420 (Fed. Cir. 1997), this term cannot be expanded to cover compounds that bear no resemblance to hyaluronic acid or a salt thereof. Consequently, the TOLMAR GEL and the method for its use in the topical treatment of actinic keratoses do not infringe any of the claims of the Solaraze patents under the doctrine of equivalents.

Furthermore, to include other common and ordinary excipients within the scope of equivalents of hyaluronic acid and salts thereof would vitiate the claim limitation in its entirety. *See Warner-Jenkins Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 39 (1997).

Moreover, dependent claims contain each and every limitation from the claims which they depend. If an independent claim is not infringed, other claims dependent upon that independent claim likewise cannot be infringed. *See Wolverine WorldWide*, 38 F.3d 1192, 1199 (Fed. Cir. 1994). Therefore, for at least the reasons set forth above, the TOLMAR GEL and the method for its use in the topical treatment of actinic keratoses do not infringe, either literally or under the doctrine of equivalents, any of the claims which depend from the independent claims of the Solaraze patents.

For at least these reasons, TOLMAR states that the manufacture, use, sale, offer for sale or import of the TOLMAR GEL does not infringe any claim of the Solaraze patents, either

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literally or under the doctrine of equivalents.

Additional Grounds For Non-Infringement Of The Solaraze Patents

Independent claim 1 of the '048 patent is directed to, *inter alia,* a method of treating a condition or disease in a human involving tissue selected from the group consisting of underperfused tissue and pathological tissue. Independent claim 2 of the '048 patent is directed to, *inter alia,* a dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating a disease and condition involving underperfused tissue and pathological tissue in humans selected from the group consisting of renal failure, cardiac insufficiency, hypertension and edema. Independent claim 5 of the '048 patent is directed to, *inter alia,* a method of treating a disease or condition involving underperfused tissue and pathological tissue in humans, wherein the disease or condition in selected from the group consisting of renal failure, cardiac insufficiency, hypertension and edema. Independent claim 1 of the '002 patent is directed to, *inter alia,* a method of treating a condition or disease in a human involving tissue selected from the group consisting of underperfused tissue and pathological tissue. Independent claim 5 of the '002 patent is directed to, *inter alia,* a method of treating infection involving underperfused tissue and pathological tissue in humans, the method comprising the administration of a therapeutically effective amount of an agent selected from the group consisting of antibiotics, antibacterials, antimicrobials and combinations thereof. Independent claim 6 of the '002 patent is directed to, *inter alia,* a method of treating infections surrounding implants involving underperfused tissue and pathological tissue in a patient, the method comprising the administration of a therapeutically effective amount of an antibiotic for the infected tissue surrounding the implant. Independent claim 10 of the '002 patent is directed to, *inter alia,* a method of (preventing) treating a topical infection resulting from a condition or disease in a human involving underperfused tissue and pathological tissue in humans, the method comprising the administration of an effective amount of an anti-metabolite agent.

Neither the TOLMAR GEL nor the TOLMAR GEL product label infringes any of the above-listed method of treating claims, either by literally, induced, contributorily or under the doctrine of equivalents.

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TOLMAR as a pharmaceutical company does not treat patients, thus there can be no direct infringement of the above-listed claims by the TOLMAR GEL.

Additionally, the TOLMAR GEL product label cannot induce or contribute to infringement of any of the above claims. The above-listed claims are directed to the treatment of diseases and conditions other than actinic keratosis. The TOMAR GEL having the same product labeling as Solaraze® diclofenac sodium 3% gel, except those changes required by law, is approved only for the treatment of actinic keratosis. Thus, there is no affirmative act by TOLMAR, which facilitates an infringing act and accordingly there can be no inducement of literal infringement of these claims. *See Beverly Hills Fan Co. v. Royal Sovereign Corp.*, 21 F.3d 1558, 1569 (Fed. Cir. 1994) (active inducement of infringement requires the commission of an affirmative act). Likewise, there can be no contributory infringement of any of the above-listed claims by TOLMAR because the indication in the TOLMAR GEL product label is not directed to these off-label uses and the TOLMAR GEL is suitable for at least one substantial non-infringing use, *e.g.*, the treatment of actinic keratosis *per se*. *See Alloc, Inc. v. U.S. Int'l Trade Comm'n*, 342 F.3d 1361, 1374 (Fed. Cir. 2003).

Independent claim 2 of the '002 patent is directed to, *inter alia*, a dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating infection involving underperfused tissue and pathological tissue in humans, said dosage amount comprising a therapeutically effective amount of an agent selected from the group consisting of antibiotics, antibacterials, antimicrobials and combinations thereof. Independent claim 4 of the '002 patent is directed to, *inter alia*, a dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for treating infections surrounding implants involving underperfused tissue and pathological tissue in a patient, said dosage amount comprising a therapeutically effective amount of an antibiotic agent for treating the infected tissue surrounding the implant. Independent claim 8 of the '002 patent is directed to, *inter alia*, a dosage amount of a pharmaceutical composition in a suitable pharmaceutically acceptable excipient for the prevention of topical infection involving underperfused tissue and pathological tissue in humans, said dosage amount comprising an effective amount of an anti-metabolite agent for preventing topical infection. Claim 5 of the '322 patent is directed to a formulation wherein

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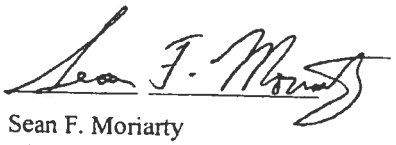
the NSAID is selected from the group consisting of ibuprofen, piroxicam, Propionic Acid derivatives, acetylsalicylic acid and Flunixin. Claim 6 of the '753 patent is directed to a pharmaceutical composition comprising, *inter alia*, novantrone. At least claims 7-12, 14-22, 24-30, 33-34, 38, 40-41, 48-53, 55-63, 65-71, 74-75, 79 and 81-82 of the '850 patent are directed to a dosage amount of a pharmaceutical composition containing, *inter alia*, an agent which is not diclofenac or a non-steriodal anti-inflammatory (NSAID). The TOLMAR GEL contains only one active ingredient, diclofenac sodium. Thus, for at least this reason, at least these claims are not literally infringed by the TOLMAR GEL. Additionally there can be no infringement under the doctrine of equivalents because the claimed agents are substantially different than diclofenac. Accordingly, for at least this reason, at least these claims are not infringed, either literally or under the doctrine of equivalents.

At least claims 31, 37, 72, 78 and 87 of the '850 patent are directed to routes of administration other than topical. The TOLMAR GEL, having the same product labeling as the Solaraze® diclofenac sodium 3% gel, except those changes required by law, is approved for topical administration only. Thus, for at least this reason, the above claims are not literally infringed by the TOLMAR GEL. Additionally, there can be no infringement under the doctrine of equivalents because topical administration is substantially different than the claimed routes of administration.. Accordingly, for at least this reason, at least these claims are not infringed, either literally or under the doctrine of equivalents.

Dated: April 8, 2010



Sean F. Moriarty
Vice President General Counsel
TOLMAR Inc.
701 Center Avenue
Fort Collins, Colorado 80526

EXHIBIT D

SkyePharma

Making good drugs better

Solaraze®

Partners: Nycomed USA, Inc & Almirall Laboratorios S.A.

A well tolerated treatment offering significant efficacy for actinic keratosis patients

Our proprietary hyaluronic acid gel technology maximises the concentration of the active drug (diclofenac) in the upper layers of the skin. This not only reduces systemic effects, but also greatly improves the efficacy of the drug. Solaraze® offers an effective and cosmetically acceptable alternative to conventional treatments that are painful or disfiguring. Solaraze® is licensed to Nycomed USA, Inc in the US, Canada & Mexico, and to Almirall S.A. in Europe and Australia. Both partners are actively involved in campaigns to raise awareness of the risks posed by this common condition and the therapeutic options available to physicians.

Solaraze® has been approved and marketed in the US and Europe for several years and recently received registration by the Australian Government (TGA). Since September 2007 it is now commercially available, through a sub-license arrangement with CSL Biotherapies, in Australia, where skin cancer has a particularly high incidence.

SkyePharma PLC is a public limited company registered in England and Wales, registration number 0107582.
Registered office: 105 Piccadilly, London, W1J 7NJ, United Kingdom

EXHIBIT E

TOLMAR Inc.

April 12, 2010

Keith Webber, PhD, Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

PATENT AMENDMENT

RE: ANDA 200936
Diclofenac Sodium Gel, 3%
Patent Amendment

Dear Director:

TOLMAR Inc. is hereby submitting a Patent Amendment to our pending Abbreviated New Drug Application for Diclofenac Sodium Gel, 3% in accordance with Section 505(j)(2)(A)(vii)(IV) of the Food, Drug and Cosmetic Act and with 21 CFR 314.94(a)(12)(i)(A)(4).

Reference is made to your communication dated March 18, 2010, stating that our ANDA 200936 for Diclofenac Sodium Gel, 3% is acceptable for filing. This application was submitted under the provisions for a Paragraph IV filing. Reference is also made to an email (attached) from Saundra Middleton of FDA stating that it is permissible to use Federal Express in lieu of the US Postal service for the purpose of providing notice to the patent holders.

In accordance with 21 CFR 314.95(b), TOLMAR Inc. certifies that notice has been provided to 1) each owner of the patent or the representative designated by the owner to receive the notice; and 2) the holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which the applicant is seeking approval. Accordingly, notice has been provided to the following:

Dr. Ken Cunningham
Chief Executive Officer
SkyePharma PLC
105 Piccadilly
London, UK
W1J 7NJ

Sarah Maxwell
Chief Operating Officer
SkyePharma U.S. Inc.
10450 Science Center Dr
San Diego, CA 92121

Paul McGarty
Chief Executive Officer
Nycomed U.S. Inc.
60 Baylis Road
Melville, NY 11747

Attn: Chief Legal Officer
SkyePharma AG
Eptingerstrasse 51
Muttenz, Switzerland
CH-4132

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Tel: 970.212.4800 - Fax 970.212.4950
www.tolmar.com

Michael Kuner
Attn: General Counsel
Nycomed International Management GmbH
Leutschenbachstrasse 95
Zurich, Switzerland
CH-8050

Attn: Chief Legal Officer
SkyePharma US, Inc.
One Broadway
14th floor
Cambridge, MA 02141

Chief Legal Officer
Jagotec AG
Eptingerstrasse 51
Muttenz, Switzerland
CH-4132
Melville, N.Y. 11747

Attn: Chief Legal Officer
PharmaDerm
210 Park Avenue
Florham Park, NJ 07932

TOLMAR Inc. certifies that the notice met the content requirements under 21 CFR 314.95(c).

In accordance with 21 CFR 314.95(e), we are providing documentation of receipt of notice by providing a copy of the FedEx proof-of-delivery (attached). The proof-of-deliveries are dated April 9, 2010 and April 12, 2010.

This ANDA is an electronic submission being submitted through the FDA Gateway system. TOLMAR Inc. certifies that the submission has been scanned for viruses using TREND MICRO Client/Server Security Agent version 9.120.1004 with current definition files and is virus free.

If there are any questions regarding this information, please contact Michelle Boyer by phone: (970) 212-4901, fax: (970) 212-4950 or email: mboyer@tolmar.com.

Sincerely,

Michelle R. Boyer
Director, Regulatory Affairs
TOLMAR Inc.

From: Middleton, Saundra T [mailto:Saundra.Middleton@fda.hhs.gov]
Sent: Monday, April 12, 2010 1:24 PM
To: Michelle Boyer
Subject: RE: Request for ANDA 200936

Dear Ms. Boyer,

Sorry for the delay.

It is permissible to use Federal Express in lieu of the US Postal service for the purpose of providing notice to the NDA holder and **any patent** assignees associated with PIV certifications contained within ANDA **200936**.

Regards,
Saundra T. Middleton
Project Manager, Regulatory Support Branch
FDA/CDER/OGD

(240) 276-8421
(240) 276-8428 (fax)
SAUNDRA.MIDDLETON@FDA.HHS.GOV

From: Michelle Boyer [mailto:MBoyer@tolmar.com]
Sent: Friday, March 26, 2010 11:49 AM
To: Middleton, Saundra T
Subject: Request for ANDA 200936

Hi Saundra,

TOLMAR has received an acceptable for filing letter for our ANDA 200936 for Diclofenac Sodium Gel, 3%, which was filed as a PIV. We are in the process of preparing the notification to the patent holder.

We are requesting to send the notification via Fed-Ex rather than certified mail. Please verify that this will be acceptable.

Thank you for your assistance.

Kind Regards,
Michelle

Michelle R. Boyer
Director, Regulatory Affairs
TOLMAR Inc.
970.212.4901
303.818.5967 (cell)

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3875 Airways Boulevard
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Telephone: 901-369-3600

April 12,2010

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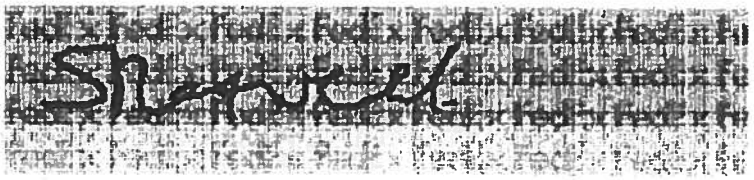

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April 9,2010

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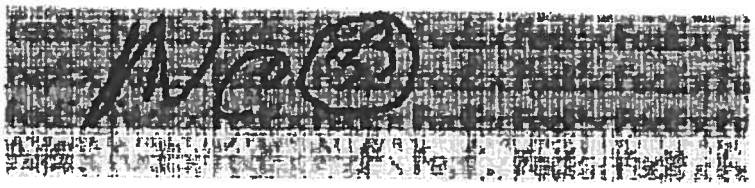
Signed for by:	. WRIGGE	**Delivery date:**	Apr 9, 2010 09:54
Service type:	Priority Envelope		



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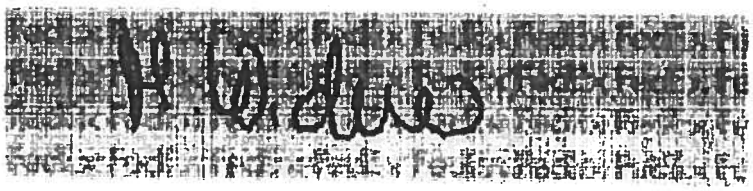
Service type:	Priority Envelope		



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Tracking number:	793428919507	**Ship date:**	Apr 8, 2010
		Weight:	1.0 lbs/0.5 kg

Recipient:
MICHAEL KUNER-ATTN: GENERAL COUNSE
NYCOMED INT. MANAGEMENT GMBH
LEUTSCHENBACHSTRASSE 95
ZURICH 8050 CH

Reference

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TOLMAR, INC.
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April 12,2010

Dear Customer:

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Signed for by:	C.GLANZMANN	**Delivery date:**	Apr 12, 2010 08:49
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April 12,2010

Dear Customer:

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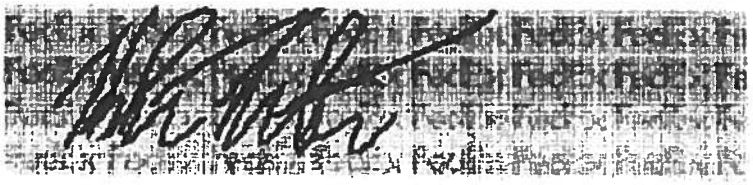
Status:	Delivered	**Delivery location:**	10450 SCIENCE CNTR DR SAN DIEGO, CA 92121
Signed for by:	H.CASTRO	**Delivery date:**	Apr 9, 2010 09:08
Service type:	Priority Envelope		



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		Weight:	0.5 lbs/0.2 kg

Recipient:
Sarah Maxwell
SkyePharma U.S. Inc.
10450 SCIENCE CENTER DR
SAN DIEGO, CA 92121 US

Shipper:
Christina Peabody
Tolmar, Inc.
701 Centre Avenue
Fort Collins, CO 80526 US

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April 12,2010

Dear Customer:

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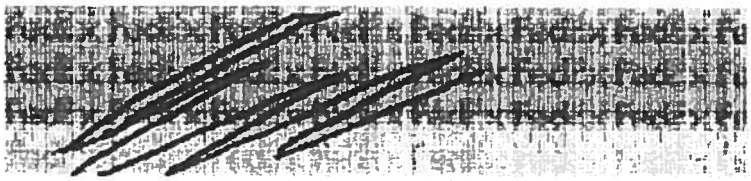

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April 9,2010

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Signed for by:	E.LO	**Delivery date:**	Apr 9, 2010 09:51
Service type:	Priority Envelope		

Shipping Information:

Tracking number:	793428851530	**Ship date:**	Apr 8, 2010
		Weight:	0.5 lbs/0.2 kg

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April 12,2010

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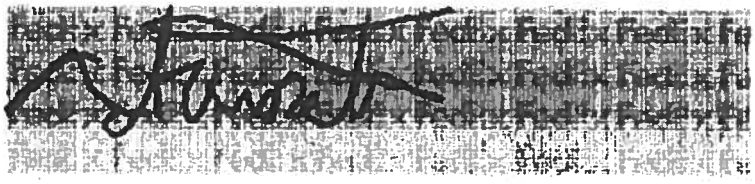
Signed for by:	.THYICHY	**Delivery date:**	Apr 12, 2010 10.07
Service type:	Priority Envelope		



Shipping Information:

Tracking number:	798551155540	**Ship date:**	Apr 8, 2010
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